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Research Article

IRRITABLE MOOD IN ADULT MAJOR DEPRESSIVE DISORDER: RESULTS FROM THE WORLD MENTAL HEALTH SURVEYS

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Background: ***Although irritability is a core symptom of DSM-IV major depressive disorder (MDD) for youth but not adults, clinical studies find comparable rates of irritability between nonbipolar depressed adults and youth. Including irritability as a core symptom of adult MDD would allow detection of depression-equivalent syndromes with primary irritability hypothesized to be more common among males than females. We carried out a preliminary examination of this***

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issue using cross-national community-based survey data from 21 countries in the World Mental Health (WMH) Surveys (n = 110,729). **Methods:** *The assessment of MDD in the WHO Composite International Diagnostic Interview includes one question about persistent irritability. We examined two expansions of the definition of MDD involving this question: (1) cases with dysphoria and/or anhedonia and exactly four of nine Criterion A symptoms plus irritability; and (2) cases with two or more weeks of irritability plus four or more other Criterion A MDD symptoms in the absence of dysphoria or anhedonia.* **Results:** *Adding irritability as a tenth Criterion A symptom increased lifetime prevalence by 0.4% (from 11.2 to 11.6%). Adding episodes of persistent irritability increased prevalence by an additional 0.2%. Proportional prevalence increases were significantly higher, but nonetheless small, among males compared to females. Rates of severe role impairment were significantly lower among respondents with this irritable depression who did not meet conventional DSM-IV criteria than those with DSM-IV MDD.* **Conclusion:** *Although limited by the superficial assessment in this single question on irritability, results do not support expanding adult MDD criteria to include irritable mood. Depression and Anxiety 30:395–406, 2013.*

Key words: *epidemiology; depression; mood disorders; assessment/diagnosis; measurement/psychometrics; irritability; major depression; nosology; world mental health (WMH) surveys*

INTRODUCTION

The diagnostic significance of irritable mood in adult major depression remains unclear. While childhood–adolescent irritability is accepted as an equivalent to dysphoria and anhedonia in diagnosing pediatric DSM-IV major depressive disorder (MDD), irritability is not included among the criteria of adult MDD. Yet, clinical studies show irritability to be more common among depressed than nondepressed patients,[1] to be at least as common in adult as pediatric MDD,[2,3] and to load on the same factor as other core symptoms of depression in factor analyses of adult depressive symptoms.[4] This age-based diagnostic inconsistency is grounded in developmental notions about the more limited expressive capacities of youth than adults[4] and in clinical concerns that adult, but not child–adolescent, irritability is a nonspecific clinical marker of a variety of disorders other than MDD.[5,6] However, scant empirical research exists on the implications of including irritability as a symptom of adult MDD.

A distinction must be made here between using irritability as a severity marker or a subtyping distinction among adults with DSM-IV MDD and using irritability to *expand* the definition of major depression. Whereas existing research suggests that irritability in MDD may serve as a severity marker in clinical samples[7,8] and have possible value as a diagnostic subtyping symptom,[4,8] we are unaware of previous evidence on the implications of allowing irritability to be used to expand the definition of adult MDD. Revising adult MDD criteria to include irritability might help offset some postulated gender bias in depression measurement, as sociocultural theories suggest that current diagnostic criteria might be insensitive to gender differences in affective expression due to men manifesting depression less than women in terms of sadness and loss of interest and more in terms of irritability.[9,10] Such an artifactual decrease in the estimated prevalence of male depression, if it exists, would be corrected by including irritability as an equivalent of dysphoria and anhedonia in assessing adult depression.

Empirical support is generally lacking for this intuitive notion of qualitative gender-related mood discrepancies, as there are inconsistent clinical reports of no gender differences in depressive irritability,[1,8,11,12] a male preponderance,[13] and a female preponderance.[2,7] Community data are rare, but recent nonrepresentative samples using college undergraduates found a female preponderance of so-called "male depression," characterized as more instrumental and aggressive symptoms.[14] Other research has suggested that depression among young males sometimes goes undetected because it manifests with irritability in the absence of reported sadness.[15]

Given that idioms of distress vary culturally, it is important to include culturally diverse samples in studies of irritability in depression.[16,17] In order to cast as wide a net as possible in this regard, we examined data from the World Mental Health (WMH) Surveys, a series of community epidemiological surveys of mental disorders carried out in 21 countries throughout the world.[18] The sample includes 110,729 adult respondents. We carried out a preliminary analysis of the extent to which expanding the list of Criterion A symptoms of DSM-IV

adult MDD to include irritability and allowing irritability to substitute for dysphoria and anhedonia as a core symptom of MDD would change prevalence estimates of DSM-IV MDD. We also examined the extent to which such changes would influence estimates of gender differences in MDD and the severity of role impairment associated with MDD. The analysis is preliminary in that only a single question about persistent irritability was included in the Composite International Diagnostic Interview (CIDI) assessment of MDD, but results could nonetheless be useful given that only limited information from other sources exists on this issue.

MATERIALS AND METHODS

SAMPLE

The WMH surveys were conducted in 22 countries, including five in countries classified by the World Bank[19] as low or lower-middle income (national surveys in Colombia and Ukraine and regional surveys in Nigeria [21 of 36 states] and the People's Republic of China [one in the Metropolitan Areas of Beijing and Shanghai and a second in the Metropolitan Area of Shenzhen]), six in countries classified as upper-middle income (national surveys in Bulgaria, Lebanon, Mexico, Romania, and South Africa, and a regional survey in Brazil [Sao Paulo Metropolitan Area]), and 11 in countries classified as high income (national surveys in Belgium, France, Germany, Israel, Italy, the Netherlands, New Zealand, Northern Ireland, Spain, and United States, and a regional survey in Japan [11 Metropolitan Areas]; Table 1). Each of the 22 surveys was administered to randomly selected respondents in a probability sample of households representative of the population.[20]

Interviews were carried out face-to-face in the homes of respondents. The 110,726 adult (age 18+) respondents who completed the survey included 28,235 in low/lower-middle income countries, 25,666 in upper-middle income countries, and 56,825 in high income countries. Individual country samples ranged from a low of 2,357 (Romania) to a high of 12,790 (New Zealand). The weighted average response rate across surveys was 71.4% (ranging from a low of 45.9% in France to a high of 87.7% in Colombia). The sample data in each country were weighted to adjust for discrepancies between the samples and population census data on a range of demographic and geographic variables.

DIAGNOSTIC ASSESSMENT

Diagnoses were based on Version 3.0 of the World Health Organization CIDI,[21] a fully structured instrument designed for use by trained lay interviewers. DSM-IV diagnostic criteria[22] were used in making diagnoses. Organic exclusions and diagnostic hierarchy rules were applied. The CIDI was developed in English and then translated, back translated, and harmonized in each country in collaboration with the WMH Data Collection Coordinating Centre (DCCC) at the University of Michigan in the United States. This was done using an expanded version of the standard WHO translation protocol.[23] Interviewers were trained by culturally competent bilingual (in English and the language(s) of the survey) supervisors in each country using consistent interviewer training materials that were standardized across surveys. Quality control protocols were also standardized and audited by DCCC staff to check interviewer accuracy and specify data cleaning and coding procedures.[24] The institutional review board of the organization that coordinated the survey in each country approved and monitored compliance with procedures for obtaining informed consent and protecting human subjects.

The CIDI assesses a wide range of disorders including major depressive episode, anxiety disorders (generalized anxiety disorder, panic disorder, agoraphobia without panic disorder, specific phobia, social phobia, posttraumatic stress disorder, adult separation anxiety disorder), intermittent explosive disorder, and substance use disorders (alcohol and drug abuse with or without dependence). The majority of surveys also assessed bipolar spectrum disorder (BP-I, BP-II, and subthreshold bipolar disorder (BPD)), but the latter disorders were not assessed in some of the initial WMH surveys. CIDI–SCID (where SCID is Structured Clinical Interview for DSM-IV) concordance using a probability subsample of WMH survey respondents from four countries found generally good concordance for these diagnoses.[25] Worst lifetime episodes are the focus of assessment. Concordance of diagnoses based on the CIDI with independent clinical diagnoses based on the SCID[26] was assessed in four WMH countries. Concordance was found to be good for major depressive episode (MDE) (area under the receiver operating characteristic curve (AUC) = 0.79), excellent for bipolar spectrum disorder (AUC = 0.94), and generally good for the other DSM-IV disorders assessed.[25]

The CIDI assessment of MDD includes several symptoms in addition to those specified in DSM-IV, including irritability, euphoria, extreme irritability, and multiple other hypomanic symptoms designed to distinguish between depressive episodes and mixed episodes. Persistent irritability is assessed with a simple yes–no query about whether the respondent was "irritable, grouchy, or in a bad mood nearly every day" during the worst 2 weeks of the index episode of sadness or anhedonia. It is possible to use responses to this question to determine how much the estimated prevalence of MDD would increase if irritability were used as an additional symptom of MDD. Specifically, respondents who did not meet lifetime criteria for bipolar spectrum disorder but who had exactly four of the requisite Criterion A symptoms of MDD were reexamined to determine whether the addition of irritability to the Criterion A symptom set would lead to a meaningful increase in the number of respondents classified as having MDD using a revised 5+ of 10 (rather than the current 5+ of 9) rule. The exclusion of respondents with a history of bipolar spectrum disorder (lifetime history of BPD, subthreshold BPD, or core hypomanic symptoms) was made based on the fact that depression with irritability could plausibly be conceptualized as a BP spectrum disorder. As noted below, though, BPD was not assessed in some countries, in which case this type of irritable depression was presumably overestimated.

In addition, we were able to explore the implications of including irritability as a *core* symptom of MDD (i.e. as a symptom that could substitute for dysphoria or anhedonia) in eight countries where a separate assessment was made of all other symptoms of MDD during episodes of being irritable among respondents who reported that they did not experience either dysphoria or anhedonia during these episodes. This assessment asked respondents whether they ever had episodes lasting 2 weeks or longer when they were "irritable, grumpy, or in a bad mood most of the day nearly every day." The requirement that this symptom last "most of the day" was imposed because DSM-IV stipulates that irritability is a substitute for dysphoria among youth and the criterion for dysphoric mood requires persistence most of the day nearly every day. We classified respondents who reported such episodes as qualifying for a definition of irritable depression if they additionally had four or more of the remaining (i.e. exclusive of dysphoria and anhedonia) seven Criterion A symptoms of MDD, again excluding respondents with a history of bipolar spectrum disorder. The eight countries in which this assessment was made included Colombia, Japan, Lebanon, Mexico, Nigeria, PRC Beijing/Shanghai, Ukraine, and the United States. A total of 43,153 respondents were included in the surveys in these eight countries.

Respondents who met criteria either for DSM-IV MDD or irritable depression in the 12 months before interview were administered a modified version of the Sheehan Disability Scales (SDS)[27] to assess severity of the role impairment caused by their depression. The SDS uses a 0–10 visual analogue scale with labels of *none* (0), *mild* (1–3),

TABLE 1. World Mental Health (WMH) Survey sample characteristics[a]

	Survey[b]	Sample characteristics[c]	Field dates	Age range	Sample size	Response rate[d]
I. Low/lower-middle income countries						
Colombia	NSMH	All urban areas of the country (approximately 73% of the total national population)	2003	18–65	(4,426)	87.7
Nigeria	NSMHW	21 of the 36 states in the country, representing 57% of the national population. The surveys were conducted in Yoruba, Igbo, Hausa, and Efik languages.	2002–3	18+	(6,752)	79.3
PRC – Beijing/Shanghai	B-WMH S-WMH	Beijing and Shanghai metropolitan areas.	2002–3	18+	(5,201)	74.7
PRC – Shenzhen	Shenzhen	Shenzhen metropolitan area. Included temporary residents as well as household residents.	2006–7	18+	(7,132)	80.0
Ukraine	CMDPSD	Nationally representative.	2002	18+	(4,724)	78.3
Total					(28,235)	
II. Upper-middle income countries						
Brazil	São Paulo Megacity	São Paulo metropolitan area.	2005–7	18+	(5,037)	81.3
Bulgaria	NSHS	Nationally representative.	2003–7	18+	(5,318)	72.0
Lebanon	LEBANON	Nationally representative.	2002–3	18+	(2,857)	70.0
Mexico	M-NCS	All urban areas of the country (approximately 75% of the total national population).	2001–2	18–65	(5,782)	76.6
Romania	RMHS	Nationally representative.	2005–6	18+	(2,357)	70.9
South Africa	SASH	Nationally representative.	2003–4	18+	(4,315)	87.1
Total					(25,666)	
III. High income countries						
Belgium	ESEMeD	Nationally representative. The sample was selected from a national register of Belgium residents	2001–2	18+	(2,419)	50.6
France	ESEMeD	Nationally representative. The sample was selected from a national list of households with listed telephone numbers.	2001–2	18+	(2,894)	45.9
Germany	ESEMeD	Nationally representative.	2002–3	18+	(3,555)	57.8
Israel	NHS	Nationally representative.	2002–4	21+	(4,859)	72.6
Italy	ESEMeD	Nationally representative. The sample was selected from municipality resident registries.	2001–2	18+	(4,712)	71.3
Japan	WMHJ2002–2006	Eleven metropolitan areas.	2002–6	20+	(4,129)	55.1
Netherlands	ESEMeD	Nationally representative. The sample was selected from municipal postal registries.	2002–3	18+	(2,372)	56.4

moderate (4–6), *severe* (7–9), and *very severe* (10) to characterize severity of impairment in each of four areas of living (work, home management, social life, close relationships). The SDS has excellent internal consistency reliability[27–29] and good concordance with objective measures of role functioning.[27–31]

ANALYSIS METHODS

Cross-tabulations estimated prevalence of irritable depression using each of the two definitions described above as well as relative prevalence versus DSM-IV/CIDI MDD. Cross-tabulations also compared rates of severe impairment assessed in the SDS of respondents with irritable

TABLE 1. Continued

	Survey[b]	Sample characteristics[c]	Field dates	Age range	Sample size	Response rate[d]
New Zealand[e]	NZMHS	Nationally representative.	2003–4	18+	(12,790)	73.3
N. Ireland	NISHS	Nationally representative.	2004–7	18+	(4,340)	68.4
Spain	ESEMeD	Nationally representative.	2001–2	18+	(5,473)	78.6
United States	NCS-R	Nationally representative.	2002–3	18+	(9,282)	70.9
Total					(56,825)	71.4
IV. Total					(110,726)	

[a]The World Bank. (2008). Data and Statistics. Accessed May 12, 2009. Available at: http://go.worldbank.org/D7SN0B8YU0

[b]NSMH (The Colombian National Study of Mental Health); IMHS (Iraq Mental Health Survey); NSMHW (The Nigerian Survey of Mental Health and Wellbeing); B-WMH (The Beijing World Mental Health Survey); S-WMH (The Shanghai World Mental Health Survey); CMDPSD (Comorbid Mental Disorders during Periods of Social Disruption); NSHS (Bulgaria National Survey of Health and Stress); LEBANON (Lebanese Evaluation of the Burden of Ailments and Needs of the Nation); M-NCS (The Mexico National Comorbidity Survey); RMHS (Romania Mental Health Survey); SASH (South Africa Health Survey); ESEMeD (The European Study Of The Epidemiology Of Mental Disorders); NHS (Israel National Health Survey); WMHJ2002–2006 (World Mental Health Japan Survey); NZMHS (New Zealand Mental Health Survey); NISHS (Northern Ireland Study of Health and Stress); NMHS (Portugal National Mental Health Survey); NCS-R (The US National Comorbidity Survey Replication).

[c]Most WMH surveys are based on stratified multistage clustered area probability household samples in which samples of areas equivalent to counties or municipalities in the United States were selected in the first stage followed by one or more subsequent stages of geographic sampling (e.g. towns within counties, blocks within towns, households within blocks) to arrive at a sample of households, in each of which a listing of household members was created and one or two people were selected from this listing to be interviewed. No substitution was allowed when the originally sampled household resident could not be interviewed. These household samples were selected from Census area data in all countries other than France (where telephone directories were used to select households) and the Netherlands (where postal registries were used to select households). Several WMH surveys (Belgium, Germany, Italy) used municipal resident registries to select respondents without listing households. The Japanese sample is the only totally unclustered sample, with households randomly selected in each of the 11 metropolitan areas and one random respondent selected in each sample household. Of the 22 surveys, 15 are based on nationally representative household samples.

[d]The response rate is calculated as the ratio of the number of households in which an interview was completed to the number of households originally sampled, excluding from the denominator households known not to be eligible either because of being vacant at the time of initial contact or because the residents were unable to speak the designated languages of the survey. The weighted average response rate is 71.4%.

[e]New Zealand interviewed respondents 16+ but for the purposes of cross-national comparisons, we limit the sample to those 18+.

depression and DSM-IV/CIDI MDD. Retrospective disorder age-of-onset reports were analyzed to estimate differential predictors of lifetime risk of irritable depression and DSM-IV/CIDI MDD in discrete time survival models with person–year the unit of analysis and a logistic link function.[32] Coefficients were exponentiated and reported as odds ratios (ORs) and 95% confidence intervals. Standard errors of all descriptive statistics were estimated using the Taylor series linearization method[33] in SAS version 9.3[34] to adjust for the weighting and clustering of WMH data. Multivariate significance of predictor sets was evaluated using Wald χ^2 tests based on design-corrected coefficient variance–covariance matrices. Statistical significance was consistently evaluated using two-sided 0.05-level tests.

RESULTS

PREVALENCE USING THE 5+ OF 10 RULE

Including irritability as an additional Criterion A symptom of MDD and using a 5+ of 10 rule instead of a 5+ of 9 rule increases the estimated lifetime prevalence of MDD by an average of 0.4% across all surveys, from 11.2 to 11.6%. (Table 2) This increase represents a 3.5% *proportional increase* over the base (i.e. 0.4/11.6 = 3.5%). The range of prevalence estimates using this definition across surveys is 0.0–1.0% (1.0–9.2% proportional increase) and the interquartile range (IQR; i.e. 25th–75th percentiles) is 0.2–0.6% (2.8–5.4% proportional increase). It should be noted that the three surveys with the highest prevalence estimates (0.9–1.0%) are among those that did not assess bipolar disorder. This means that the prevalence estimate of irritable depression is anticonservative in these countries.

The pooled average prevalence estimate across surveys is very similar for women (0.5%) and men (0.4%) and the gender difference is not significant either in any individual survey ($t = 0.0$–1.8, $P = .08$–$.93$) or in the total sample pooled across surveys ($t = 1.8$, $P = .07$). However, given that women consistently have a higher prevalence of DSM-IV MDD than men,[35] the proportional increase in total depression prevalence is for the most part (16 of 22 surveys) higher among men than women, with median (IQR) proportional increases of 5.6% (2.7–6.6) among men and 3.3% (2.2–4.3) among women. These gender differences in proportional increase are significant at the .05 level in six surveys (Nigeria, Ukraine, Mexico, Sao Paulo, Belgium, Netherlands).

PREVALENCE USING IRRITABILITY AS AN EQUIVALENT OF DYSPHORIA AND ANHEDONIA

As noted above, eight of the WMH surveys included a separate interview section that screened for lifetime episodes of irritability lasting most of the day nearly every day for 2 weeks or longer, including an assessment of all other symptoms of DSM-IV MDD during those

TABLE 2. Estimated lifetime prevalence of irritable depression using the 5+ out of 10 symptoms rule[b]

	Irritable depression						Total depression[c]						Irritable depression/total depression[d]						(n)[e]		
	Total		Male		Female		Total		Male		Female		Total		Male		Female				
	%	(SE)	%	(SE)	%	(SE)	%	(SE)	%	(SE)	%	(SE)	%	(SE)	%	(SE)	%	(SE)	Total	Male	Female
I. Low/lower-middle income countries																					
Colombia	0.4	(0.2)	0.2	(0.1)	0.6	(0.3)	12.7	(0.8)	8.8[a]	(0.8)	15.8	(1.0)	3.1	(1.3)	2.2	(1.3)	3.5	(1.9)	(4,426)	(1,700)	(2,726)
Nigeria	0.1	(0.0)	0.2	(0.1)	0.0	(0.0)	3.2	(0.3)	2.9	(0.4)	3.5	(0.4)	2.4	(1.4)	5.3[a]	(1.1)	0.0	(0.0)	(6,752)	(3,315)	(3,437)
People's Republic of China, Beijing/Shanghai[f]	0.0	(0.0)	0.0	(0.0)	0.1	(0.0)	3.6	(0.4)	3.8	(0.5)	3.3	(0.5)	1.0	(0.5)	0.0	(0.0)	2.3	(1.2)	(5,201)	(2,533)	(2,668)
People's Republic of China, Shenzhen[f]	0.2	(0.0)	0.1	(0.1)	0.3	(0.1)	6.3	(0.4)	5.8	(0.6)	6.7	(0.5)	3.1	(0.6)	2.1	(0.7)	4.0	(0.9)	(7,132)	(3,614)	(3,518)
Ukraine[f]	0.9	(0.1)	0.8	(0.2)	1.0	(0.2)	15.5	(0.7)	9.4[a]	(0.7)	20.5	(1.0)	6.1	(0.9)	8.6[a]	(2.0)	5.1	(0.7)	(4,724)	(1,792)	(2,932)
II. Upper-middle income countries																					
Bulgaria	0.6	(0.3)	0.5	(0.3)	0.6	(0.3)	6.2	(0.4)	3.7[a]	(0.7)	8.6	(0.6)	9.2	(3.9)	13.6	(6.3)	7.4	(3.6)	(5,318)	(2,430)	(2,888)
Lebanon	0.6	(0.1)	0.5	(0.2)	0.7	(0.3)	10.8	(0.9)	7.8[a]	(1.0)	13.8	(1.2)	5.4	(1.0)	6.6	(2.6)	4.8	(1.3)	(2,857)	(1,297)	(1,560)
Mexico	0.3	(0.1)	0.3	(0.2)	0.2	(0.1)	7.6	(0.5)	4.9[a]	(0.6)	10.0	(0.7)	3.1	(0.9)	5.1[a]	(0.8)	2.2	(0.7)	(5,782)	(2,285)	(3,497)
Romania	0.2	(0.1)	0.2	(0.1)	0.2	(0.1)	3.2	(0.4)	2.8[a]	(0.5)	3.6	(0.6)	6.8	(2.3)	8.7	(4.9)	5.7	(2.3)	(2,357)	(1,092)	(1,265)
São Paulo, Brazil	0.7	(0.2)	0.7	(0.2)	0.7	(0.2)	17.9	(0.8)	10.9[a]	(0.6)	24.1	(1.3)	3.6	(0.9)	5.6[a]	(1.9)	2.7	(0.7)	(5,037)	(2,187)	(2,850)
South Africa[f]	0.2	(0.1)	0.1	(0.1)	0.2	(0.1)	10.0	(0.7)	7.3[a]	(0.8)	12.3	(1.0)	1.9	(0.7)	1.9	(1.1)	2.0	(0.9)	(4,315)	(1,718)	(2,597)
III. High income countries																					
Belgium[f]	1.0	(0.4)	1.2	(0.6)	0.7	(0.3)	15.0	(1.2)	11.5[a]	(1.5)	18.5	(1.5)	6.3	(2.4)	10.2[a]	(4.3)	4.0	(1.9)	(2,419)	(1,190)	(1,229)
France[f]	0.9	(0.3)	0.5	(0.3)	1.2	(0.4)	21.9	(1.1)	15.3[a]	(1.2)	27.8	(1.4)	4.0	(1.2)	3.4	(1.9)	4.3	(1.4)	(2,894)	(1,329)	(1,565)
Germany[f]	0.4	(0.1)	0.4	(0.1)	0.4	(0.1)	10.3	(0.6)	7.6[a]	(0.8)	12.8	(0.9)	3.7	(1.0)	4.7	(1.8)	3.2	(1.1)	(3,555)	(1,660)	(1,895)
Israel	0.8	(0.1)	0.8	(0.2)	0.7	(0.2)	10.9	(0.5)	8.7[a]	(0.6)	13.0	(0.7)	6.9	(1.2)	9.0	(2.2)	5.7	(1.3)	(4,859)	(2,380)	(2,479)
Italy[f]	0.4	(0.1)	0.4	(0.2)	0.3	(0.1)	10.3	(0.5)	6.8[a]	(0.5)	13.5	(0.8)	3.5	(0.9)	5.9	(1.9)	2.3	(1.0)	(4,712)	(2,321)	(2,391)
Japan	0.3	(0.1)	0.2	(0.1)	0.3	(0.1)	6.4	(0.4)	3.8[a]	(0.5)	8.7	(0.6)	4.0	(1.2)	5.6	(2.1)	3.3	(1.3)	(4,129)	(1,868)	(2,261)
Netherlands[f]	0.5	(0.2)	0.8	(0.4)	0.3	(0.2)	18.4	(1.1)	13.7[a]	(1.5)	22.8	(1.5)	2.8	(1.1)	5.6[a]	(2.7)	1.2	(0.7)	(2,372)	(1,032)	(1,340)
New Zealand	0.4	(0.1)	0.4	(0.1)	0.4	(0.1)	17.3	(0.4)	12.4[a]	(0.6)	21.8	(0.6)	2.2	(0.4)	2.7	(0.7)	1.9	(0.4)	(12,790)	(5,537)	(7,253)
Northern Ireland	0.2	(0.1)	0.1	(0.1)	0.3	(0.1)	16.7	(0.8)	11.6[a]	(0.8)	21.6	(1.2)	1.3	(0.4)	1.0	(0.4)	1.5	(0.5)	(4,340)	(1,899)	(2,441)
Spain[f]	0.4	(0.1)	0.2	(0.1)	0.5	(0.2)	11.0	(0.5)	6.7[a]	(0.5)	15.0	(0.8)	3.5	(0.9)	3.7	(1.2)	3.4	(1.1)	(5,473)	(2,421)	(3,052)
United States	0.5	(0.1)	0.5	(0.1)	0.6	(0.1)	17.9	(0.6)	14.0[a]	(0.8)	21.6	(0.6)	2.8	(0.4)	2.9	(0.7)	2.7	(0.6)	(9,282)	(4,139)	(5,143)
IV. Total																					
Total	0.4	(0.0)	0.4	(0.0)	0.5	(0.0)	11.6	(0.1)	8.3[a]	(0.2)	14.7	(0.2)	3.5	0.2	4.3	(0.4)	(3.0)	(0.2)	(110,726)	(49,739)	(60,987)

[a]Significant gender difference at the .05 level, two-sided test.
[b]Respondents with a lifetime history of bipolar spectrum disorder were excluded from the analysis. See the text for a full description.
[c]Total depression includes both irritable depression and DSM-IV/CIDI MDD.
[d]The proportional increase in the estimated lifetime prevalence of depression if irritable depression was included along with DSM-IV/CIDI MDD.
[e]The sample sizes reported are all people included in the survey rather than those with depression. In the total sample, for example, 0.4% of the 110,729 respondents surveyed met criteria for lifetime irritable depression using the 5+ of 10 symptoms rule.
[f]Bipolar disorder was not assessed in this survey.

TABLE 3. Estimated lifetime prevalence of irritable depression based on using irritability as an equivalent of dysphoria or anhedonia[b]

	Irritable depression						Irritable depression/total depression[c] total depression[c]						Broadly defined irritable depression/total depression[d]					
	Total		Male		Female		Total		Male		Female		Total		Male		Female	
	%	(SE)	%	(SE)	%	(SE)	%	(SE)	%	(SE)	%	(SE)	%	(SE)	%	(SE)	%	(SE)
I. Low/lower-middle income countries																		
Colombia	0.2	(0.1)	0.2	(0.1)	0.1	(0.1)	1.0	(0.4)	1.7	(1.0)	0.7	(0.3)	4.0	(1.3)	3.8	(1.5)	4.2	(1.8)
Nigeria	0.0	(0.0)	0.0	(0.0)	0.0	(0.0)	0.0	(0.0)	0.0	(0.0)	0.0	(0.0)	2.4	(1.4)	5.3	(1.1)	0.0	(0.0)
PRC Beijing/Shanghai	0.2	(0.1)	0.2	(0.1)	0.2	(0.1)	4.3	(1.5)	4.3	(1.3)	4.3	(2.5)	5.2	(1.5)	4.3	(1.3)	6.5	(2.8)
Ukraine	0.1	(0.1)	0.1	(0.1)	0.1	(0.1)	0.6	(0.3)	1.2	(0.9)	0.3	(0.2)	6.6	(1.0)	9.7[a]	(2.1)	5.4	(0.8)
II. Upper-middle income countries																		
Lebanon	0.3	(0.1)	0.2	(0.2)	0.4	(0.1)	2.2	(0.9)	1.9	(1.9)	2.3	(0.8)	7.5	(1.2)	8.4	(3.1)	7.0	(1.6)
Mexico	0.2	(0.1)	0.2	(0.2)	0.2	(0.1)	2.0	(1.0)	2.8	(0.2)	1.7	(0.6)	5.1	(1.3)	7.8	(0.8)	3.8	(0.9)
III. High income countries																		
Japan	0.4	(0.1)	0.4	(0.1)	0.5	(0.2)	5.9	(1.4)	7.9	(2.7)	5.0	(1.5)	9.6	(1.8)	13.1	(3.2)	8.1	(1.9)
United States	0.4	(0.1)	0.3	(0.1)	0.5	(0.1)	2.4	(0.4)	2.7	(0.7)	2.2	(0.3)	5.1	(0.6)	5.6	(0.9)	4.8	(0.7)
IV. Total	0.2	(0.0)	0.2	(0.0)	0.3	(0.0)	2.1	(0.2)	2.6	(0.4)	1.8	(0.2)	5.5	(0.4)	6.6	(0.6)	5.0	(0.4)

[a]Significant gender difference at the .05 level, two-sided test.
[b]Respondents with a lifetime history of bipolar spectrum disorder were excluded from the analysis. See the text for a full description.
[c]The proportional increase in the estimated lifetime prevalence of depression if irritable depression was included along with DSM-IV/CIDI MDD.
[d]The proportional increase in the estimated lifetime prevalence of depression if both types of irritable depression (i.e. the type based on using the 5+ of 10 symptoms rule and the type based on using irritability as an equivalent of dysphoria or anhedonia) were included along with DSM-IV/CIDI MDD.

episodes of persistent irritability (Table 3). The mean lifetime prevalence estimate of irritable depression using the requirement of irritability plus four or more additional symptoms is 0.2% and the range (IQR) is 0.0–0.4% (0.2–0.3%), representing a proportional increase over the expanded (to include irritable depression using the 5+ of 10 rule) base of 2.1% (2.2–2.4%).

The pooled average prevalence estimate across surveys is very similar for women (0.3%) and men (0.2%), and the gender difference is not significant either in any individual survey ($t = 0.0$–1.6, $P = .11$–$.90$) or in the total sample pooled across surveys ($t = 1.1$, $P = .26$). However, as with the definition based on the 5+ of 10 symptom rule, the proportional increase in total depression due to the inclusion of this second type of irritable depression is somewhat higher among men than women, with median (IQR) proportional prevalence increases of 2.3% (1.7–2.8%) among men and 1.9% (0.7–2.3%) among women. This gender difference is not significant, though, in any of the surveys.

PREVALENCE COMBINING THE TWO DEFINITIONS

When we combine the two definitions of irritable depression, the pooled proportional mean (IQR) increase in the estimated lifetime prevalence of total major depression over the DSM-IV definition of MDD is 5.5% (5.1–6.0%) in the total sample, 6.6% (5.3–8.4%) among men, and 5.0% (4.2–6.5%) among women. The gender difference is insignificant ($t = 1.8$, $P = 0.07$).

SUBGROUP DIFFERENCES

In addition to gender differences, we examined the possibility that relative prevalence of irritable depression compared to DSM-IV/CIDI MDD varies by age, education, and country income level. We also examined gender, age, and education differences by country income level. In analyses pooled across all samples, the lower relative prevalence of irritable depression among women than men was found to be significant in high income ($\chi^2_1 = 10.8$, $P < .001$) and upper-middle income ($\chi^2_1 = 6.5$, $P = .011$) but not low/lower-middle income ($\chi^2_1 = 0.6$, $P = .45$) countries (Table 4). Age differences in relative prevalence were insignificant overall ($\chi^2_3 = 6.6$, $P = .08$) as well as in surveys carried out in each of the three country income groups ($\chi^2_3 = 2.0$–7.8, $P = .052$–$.57$), but with a trend toward higher relative prevalence among the youngest (ages 18–29) respondents. Differences by education were also insignificant overall ($\chi^2_3 = 6.3$, $P = .10$) as well as in surveys carried out in each of the country income groups ($\chi^2_3 = 3.8$–7.1, $P = .07$–$.28$). Differences by country income level, finally, were close to significant ($\chi^2_2 = 5.8$, $P = .054$) due to higher relative prevalence of irritable depression in low and middle income countries than in high income countries. Even in the subsample with the highest relative prevalence (young men in low or middle income countries), though, the marginal increase in broadly defined lifetime depression was less than 7%.

IMPAIRMENTS IN ROLE FUNCTIONING IN IRRITABLE DEPRESSION VERSUS MDD

Role impairment was assessed only for 12-month cases. Severe role impairment in at least one SDS role domain was reported by a significantly lower proportion of respondents with irritable depression than DSM-IV/CIDI MDD in the total sample (18.9 versus 43.3%,

TABLE 4. Subsample differences in relative lifetime prevalence of irritable depression versus DSM-IV/CIDI MDD

			Country income level					
	Total		High		Upper-middle		Low/lower-middle	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Gender								
Female	0.6[a]	(0.5–0.8)	0.6[a]	(0.5–0.8)	0.5[a]	(0.3–0.9)	0.8	(0.5–1.3)
Male	1.0	–	1.0	–	1.0	–	1.0	–
χ^2_1		16.2[a]		10.8[a]		6.5[a]		0.6
Age								
60+	0.8	(0.6–1.0)	1.0	(0.6–1.6)	0.4[a]	(0.2–0.8)	0.8	(0.4–1.5)
45–59	0.7[a]	(0.5–0.9)	0.7	(0.5–1.0)	0.8	(0.4–1.5)	0.7	(0.4–1.2)
30–44	0.8	(0.6–1.1)	0.8	(0.6–1.2)	0.8	(0.5–1.3)	0.9	(0.5–1.6)
18–29	1.0	–	1.0	–	1.0	–	1.0	–
χ^2_3		6.6		3.8		7.8		2.0
Education[b]								
High	1.1	(0.8–1.6)	1.4	(1.0–2.1)	0.6	(0.2–1.4)	1.1	(0.6–2.4)
High-average	0.8	(0.5–1.1)	1.0	(0.6–1.4)	0.5	(0.2–1.1)	0.4[a]	(0.2–1.0)
Low-average	1.0	(0.7–1.3)	1.1	(0.7–1.7)	0.5	(0.3–1.0)	1.0	(0.6–1.9)
Low	1.0	–	1.0	–	1.0	–	1.0	–
χ^2_3		6.3		5.7		3.8		7.1
Country income level								
Low/lower-middle	1.3	(1.0–1.7)						
Upper-middle	1.4[a]	(1.0–1.9)						
High income	1.0							
χ^2_2		5.8						
(n)		(110,726)		(56,825)		(25,666)		(28,235)

[a]Significant difference in the relative prevalence of irritable depression versus DSM-IV/CIDI MDD at the .05 level, two-sided test.
[b]Given the existence of substantial cross-national differences in educational attainment, respondents were divided roughly into quartiles in each country on the basis of level of education and pooled across countries in these categories rather than in terms of absolute number of years of education.

$t = 14.1, P < .001$). (Results not shown but available upon request.) Relative odds of severe role impairment in logistic regression models controlling for age, gender, education, and country were also significantly lower among respondents with irritable depression versus MDD and relatively consistent across the four SDS domains (OR = 0.2–0.4 across SDS role domains and 0.3 overall). Very similar patterns were found in subsamples defined by country income level, with ORs in the range 0.3–0.4 in low/lower-middle income countries, 0.3.–0.5 in upper-middle income countries, and 0.1–0.4 in high income countries (Table 5). More detailed analyses failed to find evidence of significant differences in these relative-odds based on respondent age ($\chi^2_3 = 2.0$–6.1, $P = .11$–$.57$), gender ($\chi^2_1 = 0.3$–3.0, $P = .09$–$.59$), or education ($\chi^2_3 = 1.8$–4.9, $P = .18$–$.61$). Based on these low rates of severity, the proportion of severe broadly defined cases due to irritable depression (2.1%) is even smaller than the proportion of overall broadly defined cases due to irritable depression (7.0%).

DISCUSSION

Although these results are limited by the use of a fully structured lay-administered diagnostic interview, the good concordance found between diagnoses based on the CIDI and clinical diagnoses based on blinded SCID interviews is reassuring.[25] The fact that irritability was assessed using only a single question in the MDD section about being "irritable, grouchy, or in a bad mood," though, possibly led to underreporting of true irritability, might have obscured important distinctions in types of irritability,[36,37] and could have also introduced false positives due to the ambiguity of the term "bad mood." The fact that quite a few surveys did not assess bipolar disorder could have added to the false-positive problem in leading respondents with bipolar disorder to be classified incorrectly as having irritable depression.

These limitations notwithstanding, our results show clearly that only a very small proportion of the populations in the countries studied ever meets criteria for a diagnosis of irritable depression in the absence of lifetime DSM-IV MDD. Furthermore, our finding that the prevalence of irritable depression in the absence of DSM-IV MDD does not differ markedly between men and women is inconsistent with sociocultural theories regarding irritability as a possible male equivalent of depression.[9,10,13] We found some evidence that irritable depression is more common relative to DSM-IV MDD among young men in low and middle income countries, but even in this segment of the population, there were fewer than seven cases of lifetime irritable depression for every 93 cases of lifetime DSM-IV MDD. It is certainly possible that other symptoms differentiate

TABLE 5. Severe role impairments due to 12-month irritable depression[b] versus 12-month DSM-IV/CIDI MDD[c]

	Irritable depression		DSM-IV/CIDI MDD			
	%	(SE)	%	(SE)	OR	(95% CI)
I. Total sample						
Work	7.8[a]	(1.1)	23.7	(0.6)	0.3[a]	(0.1–0.5)
Home management	6.1[a]	(1.4)	25.1	(0.7)	0.2[a]	(0.1–0.4)
Social life	11.3[a]	(1.4)	27.8	(0.7)	0.3[a]	(0.2–0.5)
Close relationships	12.4[a]	(1.4)	24.2	(0.6)	0.4[a]	(0.3–0.6)
(*n*)		(230)		(5,376)		(5,606)
II. Low/lower-middle income countries						
Work	6.0[a]	(3.0)	15.6	(1.3)	0.3	(0.1–1.0)
Home management	7.2[a]	(2.9)	20.9	(1.3)	0.3[a]	(0.1–0.7)
Social life	7.8[a]	(2.3)	16.3	(1.2)	0.4[a]	(0.2–1.0)
Close relationships	9.6[a]	(2.4)	17.8	(1.3)	0.4[a]	(0.2–1.0)
(*n*)		(59)		(1,065)		(1,124)
III. Upper-middle income countries						
Work	13.5[a]	(3.3)	28.4	(1.7)	0.4	(0.1–1.3)
Home management	8.4[a]	(3.8)	29.1	(1.5)	0.3[a]	(0.1–0.8)
Social life	20.2[a]	(3.9)	32.7	(1.5)	0.5	(0.3–1.0)
Close relationships	18.4[a]	(3.9)	30.7	(1.6)	0.5	(0.3–1.0)
(*n*)		(56)		(1,267)		(1,323)
IV. High income countries						
Work	5.4[a]	(0.2)	24.6	(0.8)	0.2[a]	(0.1–0.5)
Home management	4.5[a]	(1.1)	25.0	(0.9)	0.1[a]	(0.1–0.4)
Social life	7.9[a]	(1.5)	29.9	(0.9)	0.2[a]	(0.1–0.4)
Close relationships	10.3[a]	(1.7)	23.8	(0.8)	0.4	(0.2–0.7)
(*n*)		(115)		(3,044)		(3,159)

[a]Significant difference between irritable depression and DSM-IV/CIDI MDD in the percentage of cases with severe role impairment.
[b]Irritable depression was defined broadly to include both the type based on using the 5+ of 10 symptoms rule and, in the eight surveys that included a separate interview section on episodes of persistent irritability, the type based on using irritability as an equivalent of dysphoria or anhedonia.
[c]Based on a logistic regression model with a dummy predictor variable for irritable depression (coded 1) versus DSM-IV/CIDI MDD (coded 0) predicting a dichotomous outcome for severity of role impairment controlling for respondent age, gender, education, and country.

male from female depression that need to be elucidated in future research, but the results presented here are inconsistent with the notion that irritability is central to such differences.

We also found that irritable depression is associated with substantially less role impairment than DSM-IV MDD, resulting in there being only about two cases of severely impairing lifetime irritable depression for every 98 cases of severely impairing lifetime DSM-IV MDD. One possible explanation for this finding of lower levels of severe impairment in irritable depression than DSM-IV depression might be that the cases of irritable depression might include a high proportion of respondents who met all criteria for mania or hypomania other than the requirement for marked impairment in mania (DSM-IV Criterion D) or clinically significant impairment in hypomania (DSM-IV Criterion E). This was not the case, though, as such cases were removed from the analysis at the onset when we excluded respondents with core hypomanic symptoms in an effort to avoid this kind of confounding.

It is noteworthy that despite the very small number of respondents who met criteria for irritable depression in the absence of DSM-IV MDD, a majority of WMH respondents with a history of MDD report irritability during their depressive episodes.[35] This is consistent with the finding in numerous clinical studies that a high proportion of adult patients in treatment for MDD have symptoms of irritability.[2,5–7,38–41] It also ties in with the point made in the introduction that irritability might be a useful severity marker[7,8] or a useful basis for subtyping adults with DSM-IV MDD[4,8] even if it is not a useful basis for expanding the definition of MDD. It might be the case that information about irritability has relevance for depression treatment. In interpreting the results of our study, it is important to be clear that we are addressing only the issue of expanding the definition of MDD and not issues of subtyping or distinguishing the severity of threshold cases of MDD.

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